HETEROCYCLES, Vol. 87, No. 1, 2013, pp. 177 - 191. © 2013 The Japan Institute of Heterocyclic Chemistry
Received, 31st October, 2012, Accepted, 14th November, 2012, Published online, 22nd November, 2012
DOI: 10.3987/COM-12-12615

A NOVEL ONE-STEP SYNTHESIS OF BENZO[*b*]FURO[3,2-*b*]PYRIDINES HAVING AN AMINO GROUP AT THE 4-POSITION FROM BENZO[*b*]FURO[3,2-*d*][1,3]OXAZINE

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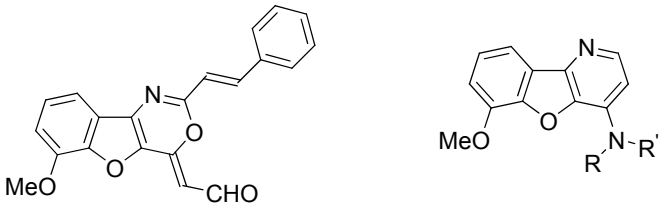
Abstract – A novel one-step synthesis of benzo[*b*]furo[3,2-*b*]pyridines having an amino group at the 4-position from benzo[*b*]furo[3,2-*d*][1,3]oxazine by treatment of various amines is described.

Benzo[*b*]furan derivatives with a fused pyridine ring show various bioactivities, for example, antibacterial activity,[1] inhibition of gyrase,[2] and affinity for the adenosine A_3 receptor.[3] From them, benzo[*b*]furo[3,2-*b*]pyridine with an amino group at the 4-position has been found as a basic structure of several compounds showing activity against malaria.[4] We have been interested in the preparation of benzo[*b*]furan derivatives and their biological activities, and have reported several pharmaceutically interesting compounds with activities, such as cysteinyl leukotriene 2 receptor antagonistic activity[5] activity against human leukotriene B_4 (BLT_1, BLT_2) receptors,[6] poly(ADP-ribose)polymerase-1 inhibitory activity,[7] and growth inhibitory activity toward human pancreatic cancer cells.[8]

In continuing our research, we prepared several compounds having the benzo[*b*]furo[3,2-*d*][1,3]oxazine skeleton, and some of them showed anti-osteoclastic bone resorption activity,[9] selective estrogen receptor modulators and growth inhibitory activity toward cancer cells.[10] During our research program preparing benzo[*b*]furo[3,2-*d*][1,3]oxazine derivatives, we discovered a novel one-step conversion from benzo[*b*]furo[3,2-*d*][1,3]oxazine to benzo[*b*]furo[3,2-*b*]pyridine derivatives with an amino group at the

4-position. Although several examples of conversion into a pyridine-fused polycyclic system from 1,3-oxazine derivatives have been reported,[11] the products of these reactions were mostly 4-hydroxypyridine derivatives,[11c-g] and preparation of 4-aminobenzo[*b*]furo[3,2-*b*]pyridine derivatives from 1,3-oxazine compounds by one-step conversion remains unknown.

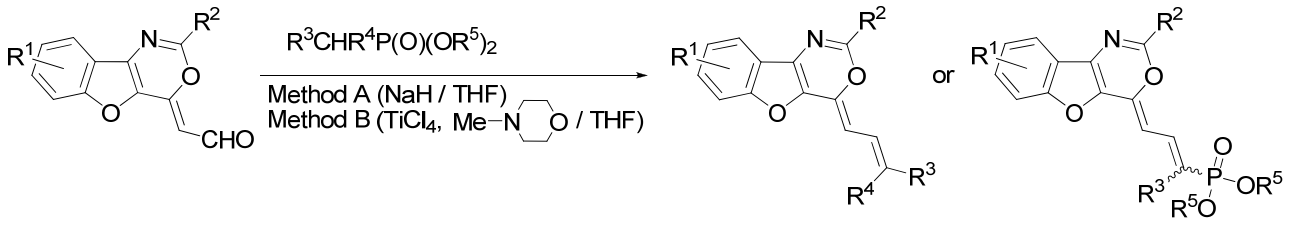
In this paper, we report a novel one-step conversion into 4-aminobenzo[*b*]furo[3,2-*b*]pyridine derivatives **2** from (*Z*)-4-ylidenebenzo[*b*]furo[3,2-*d*][1,3]oxazine **1,** which could be easily prepared on a multi-gram scale.[10]



1 **2**

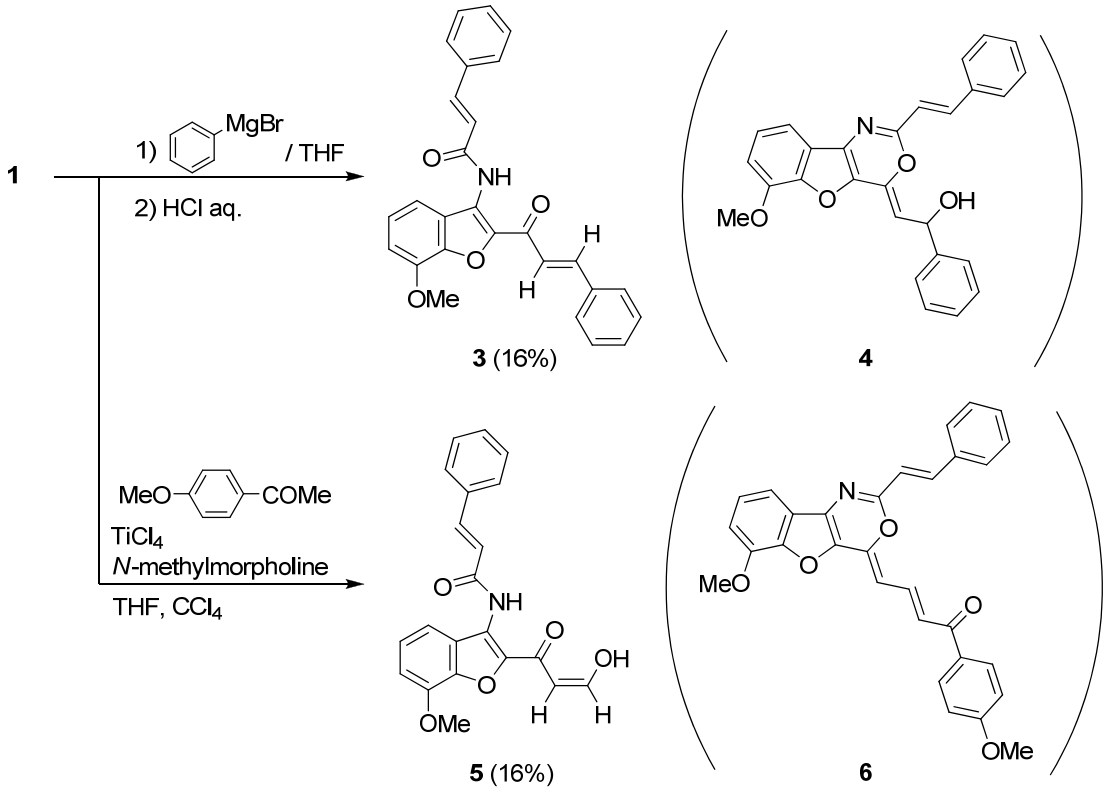
Figure 1

In previous papers, we have reported the preparation of several butadiene derivatives containing the benzo[*b*]furo[3,2-*d*][1,3]oxazine skeleton from **1**, by reaction with phosphonate reagents in the presence of NaH or $TiCl_4$ (Scheme 1).[9,10]



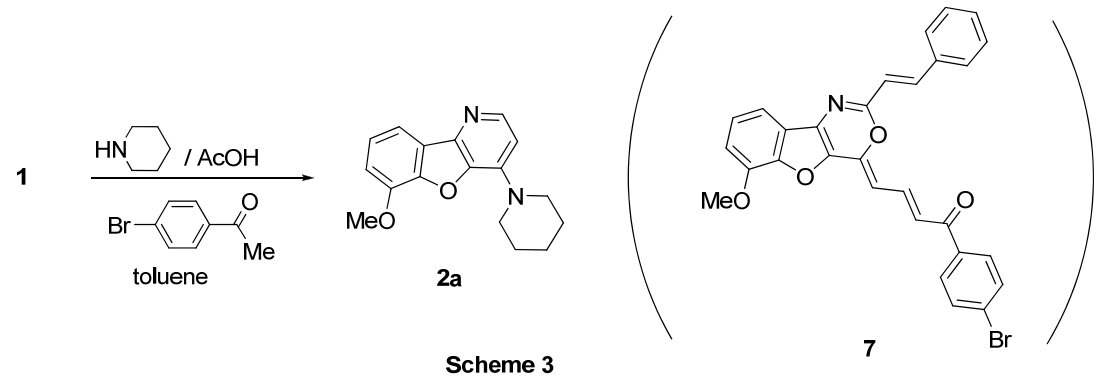
Scheme 1

In order to prepare other types of derivatives from **1**, several reaction conditions were tried as shown in Scheme 2. Treatment of aldehyde **1** with phenylmagnesium bromide or *p*-methoxyacetophenone in the presence of $TiCl_4$ and *N*-methylmorpholine afforded the ketoamide **3** or the enol ketone **5** by opening of the oxazine ring, but benzo[*b*]furo[3,2-*d*][1,3]oxazine derivatives **4** or **6** could not be found in these reaction mixtures.



Scheme 2

We supposed that the oxazine ring of benzo[*b*]furo[3,2-*d*][1,3]oxazine **1** could easily open under acidic conditions, and tested the condensation under neutral reaction conditions. A reaction of aldehyde **1** with *p*-bromoacetophenone in the presence of piperidine and acetic acid gave 6-methoxy-4-(piperidin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine **2a** without the expected condensation product **7**. The structure of a new compound **2a** has been supported by ^{1}H-NMR, ^{13}C-NMR, EIMS, IR and elemental analysis data. In addition, HMBC experiments led to the indicated structure of the obtained product **2a** having a benzo[*b*]furo[3,2-*b*]pyridine skeleton, as shown in Figure 2.



Scheme 3

HMBC of **2a**

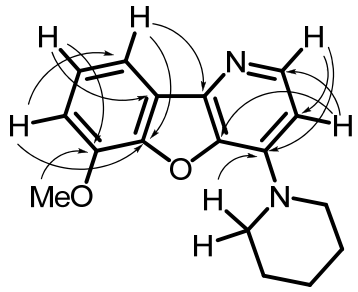
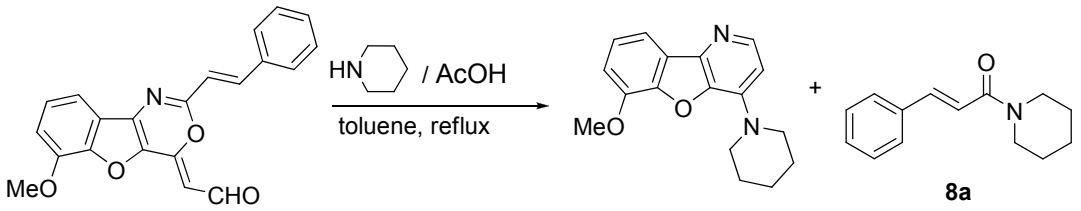


Figure 2

We decided therefore to investigate this one-step conversion to 6-methoxy-4-(piperidin-1-yl)benzo[*b*]-furo[3,2-*b*]pyridine **2a** from (*Z*)-(6-methoxy-(*E*)-2-styrylbenzo[*b*]furo[3,2-*d*][1,3]oxazin-4-ylideno)-acetaldehyde **1**. The optimized reaction conditions to give **2a** were examined as shown in Table 1. Reactions of **1** with piperidine (2.2 equiv.) in the presence of acetic acid (1.1, 0.5, 0.2 equiv.) in toluene afforded **2a** in yields of 34, 38, and 61%, respectively. Also obtained was 1-cinnamoylpiperidine **8a**. The reaction conditions in the absence of acetic acid were then examined. When two equivalents of piperidine without acetic acid were used, the desired product **2a** was obtained in the highest yield (85%).



1 **2a** **8a**

Table 1

Entry	HN	AcOH	Yield (%)	
			2a	**8a**
1	2.2 eq.	1.1 eq.	34	61
2	2.2 eq.	0.5 eq.	38	50
3	2.2 eq.	0.2 eq.	61	54
4	1.0 eq.	\	22	34
5	2.0 eq.	\	85	82
6	3.0 eq.	\	83	83
7	4.0 eq.	\	74	77

Benzo[*b*]furo[3,2-*d*][1,3]oxazine compound **1** was treated with various secondary or primary amines under the optimal reaction conditions to afford the corresponding benzo[*b*]furo[3,2-*b*]pyridine derivatives

with an amino group at the 4-position, and the results are summarized in Table 2. Several kinds of amine were successfully reacted with **1** to give 4-aminobenzo[*b*]furo[3,2-*b*]pyridines **2** in moderate to high yields.

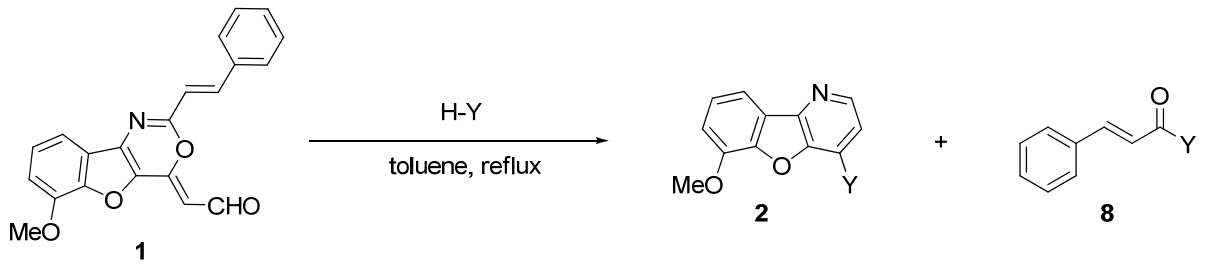
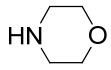
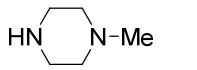
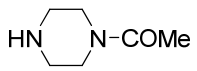
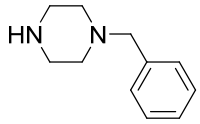
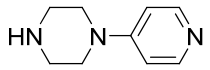
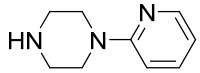
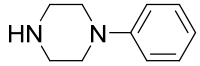
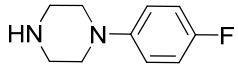
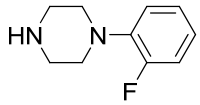
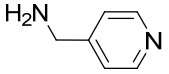
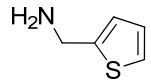
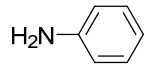
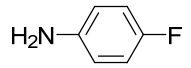
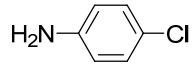
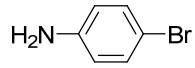
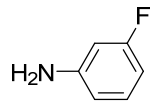
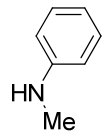


Table 2

	amine H–Y	Yield (%) 2	Yield (%) 8
b		80 (**2b**)	88 (**8b**)[12]
c		84 (**2c**)	91 (**8c**)[13]
d		66 (**2d**)	83 (**8d**)
e		58 (**2e**)	86 (**8e**)[13]
f		90 (**2f**)	46 (**8f**)
g		78 (**2g**)	75 (**8g**)
h		49 (**2h**)	72 (**8h**)[14]
i		66 (**2i**)	77 (**8i**)
j		57 (**2j**)	89 (**8j**)
k	$HNEt_2$	64 (**2k**)	64 (**8k**)[12]
l		45 (**2l**)	52 (**8l**)[15]
m		65 (**2m**)	68 (**8m**)
n		94 (**2n**)	82 (**8n**)[12]
o		50 (**2o**)	59 (**8o**)[16]
p		50 (**2p**)	37 (**8p**)[12]
q		51 (**2q**)	50 (**8q**)[17]
r		65 (**2r**)	71 (**8r**)[18]
s		63 (**2s**)	73 (**8s**)[19]

The proposed reaction mechanism for the formation of the benzo[*b*]furo[3,2-*b*]pyridine **2a** from benzo[*b*]furo[3,2-*d*][1,3]oxazine **1** is shown in Figure 3. The aldehyde group of **1** reacted with the amine to form the iminium intermediate **A**. Adding one more molecule of the amine to the C-4 of **A** led to opening of the oxazine ring of **B** to give **C**. The dihydropyridine ring was formed by conjugate addition of amide nitrogen in **C**, and then, elimination of cinnamaminde from **D** by aromatization afforded benzo[*b*]furo[3,2-*b*]pyridines **2**.

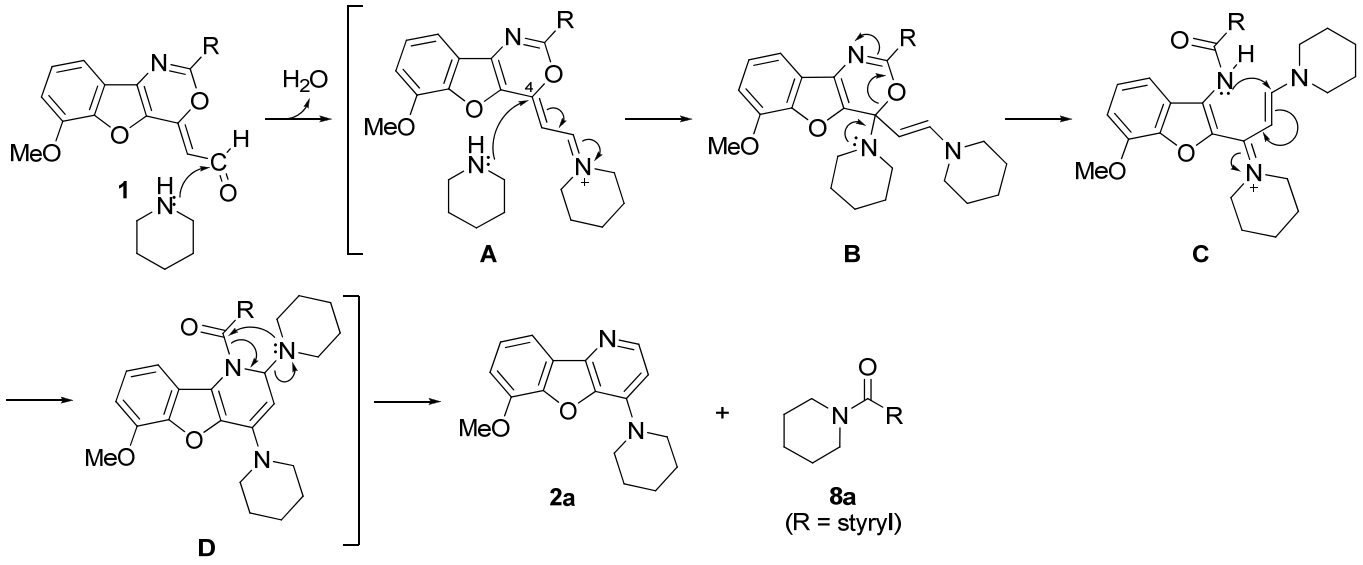


Figure 3

In conclusion, we developed a novel one-step synthesis of benzo[*b*]furo[3,2-*b*]pyridines with an amino group attached at the 4-position from benzo[*b*]furo[3,2-*d*][1,3]oxazine compounds. We are currently investigating the scope of this reaction and applications toward biologically active compounds.

EXPERIMENTAL

Melting points were measured with a Yanaco MP micro-melting-point apparatus and are uncorrected. NMR spectra were measured on JEOL JNM-ECP500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) or JEOL JNM-ECP400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), and the chemical shifts were expressed in parts per million (ppm) downfield from tetramethylsilane as the internal standard. Mass spectra were measured on a JEOL JMS DX-303 EI-MS spectrometer. Elemental analyses were performed on a CHN CORDER MT-3 (Yanaco). Silica gel (Merck Art. 7734) for column chromatography and Silica gel 60 PF_{254} (Nacalai Tesque Inc.) for preparative TLC (PTLC) were used.

***N*-(2-Cinnamoyl-7-methoxybenzofuran-3-yl)cinnamamide (3)**: Phenylmagnesium bromide (32% in THF, 1.08 mL, 2.1 mmol) was added to a stirred solution of **1**[10] (0.20 g, 0.58 mmol) in THF (80 mL) under N_2 at 0 ˚C, and the mixture was refluxed for 6 h. The reaction mixture was poured into water and acidified with 10% hydrochloric acid, then the solvent was concentrated under reduced pressure. The products were extracted with $CHCl_3$, washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by column chromatography ($CHCl_3$/AcOEt 10:1) and recrystallized from $CHCl_3$/AcOEt to give **3** (0.04 g, 16%) as a yellow solid; mp 212.8-214.1 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.06 (3H, s, OCH_3), 6.76 (1H, d, *J* = 15.4 Hz, PhCH=C*H*), 7.03 (1H, dd, *J* = 8.1 and 0.8 Hz, Bf 4 or 6-H), 7.25 (1H, t, *J* = 8.3 Hz, Bf 5-H), 7.40-7.46 (6H, m, Ph-H), 7.60-7.63 (2H, m,

Ph-H), 7.72-7.76 (3H, m, Ph-H), 7.74 (1H, d, *J* = 15.8 Hz, PhCH=C*H*), 7.84 (1H, d, *J* = 15.8 Hz, PhC*H*=CH), 7.94 (1H, d, *J* = 15.7 Hz, PhC*H*=CH), 8.30 (1H, dd, *J* = 8.5 and 0.8 Hz, Bf 4 or 6-H), 10.93 (1H, s, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.1, 110.5, 119.8, 120.5, 121.2, 122.9, 123.6, 128.2, 129.0, 129.0, 130.3, 130.9, 132.8, 134.5, 134.7, 139., 143.5, 144.4, 144.9, 145.7, 163.7, 182.2; MS (EI) *m/z*: 423 (M^+, 67), 293 (64), 216 (56), 131 (100), 103 (37); Anal. Calcd for $C_{27}H_{21}NO_4 \cdot 1/2H_2O$; C, 74.99; H, 5.13; N, 3.24. Found; C, 4.84; H, 5.13; N, 3.22.

***N*-(2-((*Z*)-3-Hydroxyacryloyl)-7-methoxybenzofuran-3-yl)cinnamamide (5)**: A solution of titanium(IV) chloride (120 μL, 1.18 mmol) in CCl_4 (20 mL) was added to a stirred solution of 4'-methoxyacetophenone (43.5 mg, 0.29 mmol) in THF (4 mL) under N_2 at 0 ˚C, then (*Z*)-(6-methoxy-(*E*)-2-styrylbenzo[*b*]furo[3,2-*d*][1,3]oxazin-4-ylideno)acetaldehyde **1** (0.10 g, 0.29 mmol) in anhydrous THF (80 mL) and *N*-methylmorpholine (254 μL, 2.32 mmol) were added to the reaction mixture. The reaction mixture was stirred 67 h at room temperature, then poured into water and the solvent was concentrated under reduced pressure. The products were extracted with $CHCl_3$, washed with brine, and dried over $MgSO_4$, then the solvent was removed under reduced pressure. The crude residue was recrystallized from hexane/AcOEt to give **5** (0.0173 g, 16%) as a yellow solid; mp 146.0-148.0 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.02 (3H, s, OCH_3), 6.37 (1H, d, *J* = 5.6 Hz, C*H*=CHOH or CH=C*H*OH), 6.70 (1H, d, *J* = 15.9 Hz, PhCH=C*H*), 6.99 (1H, dd, *J* = 2.2 and 0.8 Hz, 4 or 6-H), 7.22 (1H, t, *J* = 8.2 Hz, 5-H), 7.40 - 7.44 (3H, m, Ph-H), 7.59 (1H, d, *J* = 5.1 Hz, C*H*=CHOH or CH=C*H*OH), 7.61-7.63 (2H, m, Ph-H), 7.83 (1H, d, *J* = 15.3 Hz, PhC*H*=CH), 8.21 (1H, dd, *J* = 8.2 and 1.0 Hz, 4 or 6-H), 10.43 (1H, s, NH), 14.09 (1H, br s, OH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.1, 99.4, 110.5, 119.6, 120.3, 123.0, 123.6, 128.2, 128.9, 130.3, 132.0, 134.4, 136.5, 143.7, 145.1, 145.6, 163.5, 169.4, 185.8; MS (EI) *m/z*: 363 (M^+, 25), 233 (15), 131 (100), 103 (56), 77 (28); HRMS (EI) *m/z*: 363.1105 (Calcd for $C_{21}H_{17}NO_5$, 363.1107).

Preparation of benzo[*b*]furo[3,2-*b*]pyridines and cinnamamides: General Procedure

A solution of **1** (0.10 g, 0.290 mmol) and 2 equiv of amines in toluene (2.9 mL or 40 mL) was refluxed for 1-9 h (TLC monitoring). The solvent was evaporated off and the residue was purified by PTLC and recrystallized from hexane-AcOEt.

In the case of **2k** and **2m**, 20 equiv of diethylamine and 6 equiv of 2-thiophenylmethanamine were used, respectively.

6-Methoxy-4-piperadinobenzo[*b*]furo[3,2-*b*]pyridine (2a): PTLC with [$CHCl_3$/AcOEt (5:2)]; pale yellow solid; yield 85%; mp 109.7-111.8 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.69-1.82 (6H, m, piperidine 3, 4, 5-H), 3.69 (4H, t, *J* = 5.4 Hz, piperidine 2, 6-H), 4.06 (3H, s, OCH_3), 6.69 (1H, d, *J* = 5.9 Hz, 3-H), 7.03 (1H, dd, *J* = 8.1 and 1.1 Hz, 7-H), 7.30 (1H, t, *J* = 7.9 Hz, 8-H), 7.76 (1H, dd, *J* = 7.7 and 1.1 Hz,

9-H), 8.32 (1H, d, *J* = 5.9 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 24.5 (piperidine C4), 25.6 (OCH_3), 49.4 (piperidine C3, 5), 56.3 (piperidine C2, 6), 107.0 (C3), 110.7 (C7), 113.1 (C9), 123.9 (C8), 125.7 (C9a), 140.0 (C4a), 142.9 (C4), 144.3 (C9b), 145.3 (C5a), 145.7 (C6), 146.6 (C2); IR (KBr) ν: 2928, 1632, 1594, 1410, 1267, 1178 cm^{-1}; MS (EI) *m/z*: 282 (M^+, 100), 241 (11), 226 (18), 198 (2); Anal. Calcd for $C_{17}H_{18}N_2O_2 \cdot 2/3\ H_2O$: C, 69.37; H, 6.62; N, 9.52. Found: C, 69.18; H, 6.40; N, 9.42.

6-Methoxy-4-morpholinobenzo[*b*]furo[3,2-*b*]pyridine (2b): PTLC with [$CHCl_3$/AcOEt (5:2)]; pale yellow solid; yield 80%; mp 177.1-180.7 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.67 (4H, t, *J* = 4.8 Hz, morpholine 3, 5-H), 3.95 (4H, t, *J* = 4.8 Hz, morpholine 2, 6-H), 4.04 (3H, s, OCH_3), 6.69 (1H, d, *J* = 5.9 Hz, 3-H), 7.04 (1H, dd, *J* = 8.1 and 0.7 Hz, 7-H), 7.32 (1H, t, *J* = 7.9 Hz, 8-H), 7.78 (1H, dd, *J* = 7.9 and 0.9 Hz, 9-H), 8.37 (1H, d, *J* = 5.9 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 48.3, 56.1, 66.7, 106.6, 110.7, 113.0, 124.1, 125.3, 142.5, 144.5, 145.4, 145.7, 146.7; IR (KBr) ν: 1597, 1273, 1202, 1120, 987 cm^{-1}; MS (EI) *m/z*: 284 (M^+, 85), 226 (100), 211 (16), 198 (2), 183 (17); Anal. Calcd for $C_{17}H_{16}N_2O_3 \cdot 9/10\ H_2O$: H, 6.07; C, 64.00; N, 9.27. Found: H, 5.81; C, 63.94; N, 9.23.

6-Methoxy-4-(4-methylpiperazin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine (2c): PTLC with [$CHCl_3$/MeOH (5:2) and MeOH]; white solid; yield 84%; mp 157.0-158.5 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.38 (3H, s, CH_3), 2.66 (4H, t, *J* = 5.1 Hz, piperazine-H), 3.73 (4H, t, *J* = 5.0 Hz, piperazine-H), 4.05 (3H, s, OCH_3), 6.69 (1H, d, *J* = 5.9 Hz, 3-H), 7.04 (1H, dd, *J* = 8.0 and 1.1 Hz, 7-H), 7.32 (1H, t, *J* = 7.9 Hz, 8-H), 7.77 (1H, dd, *J* = 7.9 and 0.9 Hz, 9-H), 8.36 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 46.1, 47.8, 54.7, 56.0, 106.8, 110.5, 112.9, 123.8, 125.3, 139.8, 142.3, 144.2, 145.2, 145.5, 146.5; IR (KBr) ν: 2799, 1594, 1461, 1267, 1178, 1086 cm^{-1}; MS (EI) *m/z*: 297 (M^+, 100), 282 (22), 255 (23), 226 (68), 70 (89); Anal. Calcd for $C_{17}H_{19}N_3O_2 \cdot 1/5H_2O$: C, 67.84; H, 6.50; N, 13.96. Found: C, 68.10; H, 6.40; N, 13.81.

6-Methoxy-4-(4-acetylpiperazin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine (2d): PTLC with [$CHCl_3$/MeOH (5:2) and MeOH]; pale yellow solid; yield 66%; mp 192.5-194.3 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.17 (3H, s, $COCH_3$), 3.62-3.89 (8H, m, piperazine-H), 4.06 (3H, s, OCH_3), 6.70 (1H, d, *J* = 5.5 Hz, 3-H), 7.06 (1H, dd, *J* = 8.1 and 0.7 Hz, 7-H), 7.34 (1H, t, *J* = 7.9 Hz, 8-H), 7.77 (1H, dd, *J* = 7.9 and 1.0 Hz, 9-H), 8.39 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 21.2, 40.9 (CH_2), 45.9 (CH_2), 47.5 (CH_2), 48.1 (CH_2), 56.0, 106.9, 110.6, 112.9, 124.1, 125.2, 139.7, 141.8, 144.5, 145.3, 145.6, 146.6, 169.0; IR (KBr) ν: 3010, 1649, 1594, 1430, 1249, 1191 cm^{-1}; MS (EI) *m/z*: 325 (M^+, 58), 282 (20), 253 (100), 240 (33), 226 (27), 212 (22), 56 (37), 43 (30); Anal. Calcd for $C_{18}H_{19}N_3O_3 \cdot 1/4\ H_2O$: C, 65.54; H, 5.96; N, 12.74. Found: C, 65.83; H, 5.93; N, 12.49.

(*E*)-1-(4-Acetylpiperazin-1-yl)-3-phenylprop-2-en-1-one (8d): pale yellow oil; yield 83%; ^{1}H-NMR

(400 MHz, $CDCl_3$) δ: 2.14 (3H, s, $COCH_3$), 3.51-3.75 (8H, m, piperazine-H), 6.85 (1H, d, *J* = 15.4 Hz, PhCH=C*H*), 7.36-7.40 (3H, m, Ph-H), 7.52-7.54 (2H, m, Ph-H), 7.71 (1H, d, *J* = 15.4 Hz, PhC*H*=CH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 21.2, 41.3, 46.0, 116.4, 127.7, 128.7, 129.7, 134.9, 143.4, 165.6, 169.1; IR (KBr) ν: 2922, 1645, 1430, 1219, 997 cm^{-1}; MS (EI) *m/z*: 258 (M^+, 47), 243 (14), 131 (100), 103 (63), 85 (84), 77 (38); HRMS (EI) *m/z*: 258.1370 (Calcd for $C_{15}H_{18}FN_2O_2$, 258.1368).

4-(4-Benzylpiperazin-1-yl)-6-methoxybenzo[*b*]furo[3,2-*b*]pyridine (2e): PTLC with [hexane/AcOEt (1:10)]; yellow solid; yield 58%; mp 63.3-65.8 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.69 (4H, t, *J* = 4.9 Hz, piperazine), 3.60 (2H, s, PhCH_2), 3.72 (4H, t, *J* = 5.2 Hz, piperazine), 4.03 (3H, s, OCH_3), 6.67 (1H, d, *J* = 5.9 Hz, 3-H), 7.03 (1H, dd, *J* = 8.1 and 0.8 Hz, 7-H), 7.28-7.39 (6H, m, 8-H, Ph-H), 7.76 (1H, dd, *J* = 7.9 and 0.9 Hz, 9-H), 8.34 (1H, d, *J* = 5.8 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 48.0, 52.8, 56.1, 63.1, 106.8, 110.7, 113.0, 123.9, 125.4, 127.2, 128.3, 129.2, 137.7, 139.9, 142.5, 144.2, 145.3, 145.7, 146.5; IR (KBr) ν: 2956, 1594, 1458, 1437, 1270, 1198 cm^{-1}; MS (EI) *m/z*: 373 (M^+, 100), 282 (18), 227 (80), 146 (29), 91 (50); Anal. Calcd for $C_{23}H_{23}N_3O_2 \cdot 1/2\ H_2O$: C, 67.46; H, 6.65; N, 10.26. Found: C, 67.42; H, 6.69; N, 10.28.

6-Methoxy-4-(4-(pyridin-4-yl)piperazin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine (2f): PTLC with [$CHCl_3$/AcOEt (5:2) and MeOH]; white solid; yield 90%; mp 224.0-225.0 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.60-3.62 (4H, m, piperazine-H), 3.86-3.88 (4H, m, piperazine-H), 4.07 (3H, s, OCH_3), 6.73 (1H, d, *J* = 5.5 Hz, 3-H), 6.74 (2H, dd, *J* = 5.0 and 1.7 Hz, pyridine), 7.06 (1H, dd, *J* = 7.9 and 0.9 Hz, 7-H), 7.34 (1H, t, *J* = 7.9 Hz, 8-H), 7.78 (1H, dd, *J* = 7.9 and 0.9 Hz, 9-H), 8.34 (2H, dd, 4.8 and 1.5 Hz, pyridine), 8.40 (1H, d, *J* = 5.8 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 45.8, 47.4, 56.1, 106.8, 108.5, 110.7, 113.0, 124.2, 125.3, 139.8, 141.9, 144.7, 145.4, 145.7, 146.7, 150.5, 154.7; IR (KBr) ν: 1591, 1512, 1406, 1243, 1202 cm^{-1}; MS (EI) *m/z*: 360 (M^+, 100), 226 (44), 133 (35), 106 (37); Anal. Calcd for $C_{21}H_{20}N_4O_2 \cdot 5/6H_2O$: C, 66.02; H, 5.91; N, 14.67. Found: C, 66.20; H, 5.79; N, 14.53.

(*E*)-3-Phenyl-1-(4-(pyridin-4-yl)piperazin-1-yl)prop-2-en-1-one (8f): pale yellow solid; yield 46%; mp 136.0-138.4 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.40-3.43 (4H, m, piperazine-H), 3.85 (4H, br s, piperazine-H), 6.67 (2H, d, *J* = 6.2 Hz, pyridine 3, 5-H), 6.88 (1H, d, *J* = 15.3 Hz, PhCH=C*H*), 7.36-7.41 (3H, m, Ph-H), 7.52-7.55 (2H, m, Ph-H), 7.72 (1H, d, *J* = 15.4 Hz, PhC*H*=CH), 8.32 (2H, d, *J* = 5.9 Hz, pyridine 2, 6-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 41.5, 44.9, 45.9, 108.4, 116.5, 127.8, 128.8, 129.8, 135.0, 143.4, 150.3, 154.5, 165.6; IR (KBr) ν: 1645, 1594, 1441, 1226, 990 cm^{-1}; MS (EI) *m/z*: 293 (M^+, 76), 202 (20), 162 (51), 133 (100), 131 (56), 103(47); Anal. Calcd for $C_{18}H_{19}N_3O \cdot 1/5\ H_2O$: C, 72.80; H, 6.58; N, 14.15. Found: C,73.06; H, 6.55; N, 13.98.

6-Methoxy-4-(4-(pyridin-2-yl)piperazin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine (2g): PTLC with

[hexane/AcOEt (1:2)]; pale yellow solid; yield 78%; mp 132.8-135.7 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.80-3.87 (8H, m, piperazine), 4.07 (3H, s, OCH_3), 6.67-6.72 (2H, m, 3', 5'-H), 6.74 (1H, d, *J* = 5.5 Hz, 3-H), 7.05 (1H, d, *J* = 8.1 Hz, 7-H), 7.33 (1H, t, *J* = 7.9 Hz, 8-H), 7.53 (1H, ddd, *J* = 8.6, 7.0 and 1.9 Hz, 4'-H), 7.78 (1H, dd, *J* = 7.7 and 1.1 Hz, 9-H), 8.24 (1H, dd, *J* = 4.9 and 2.0 Hz, 6'-H), 8.38 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 45.0, 47.7, 56.1, 106.8, 107.1, 110.7, 113.0, 113.7, 124.0, 125.4, 137.5, 139.8, 142.2, 144.4, 145.3, 145.7, 146.6, 148.0, 159.2; IR (KBr) ν: 1587, 1434, 1270, 1239 cm^{-1}; MS (EI) *m/z*: 360 (M^+, 48), 254 (100), 227 (42), 107 (71); Anal. Calcd for $C_{21}H_{20}N_4O_2 \cdot 1/4\ H_2O$: C, 69.12; H, 5.66; N, 15.35. Found: C, 69.23; H, 5.50; N, 15.20.

(*E*)-3-Phenyl-1-(4-(pyridin-2-yl)piperazin-1-yl)prop-2-en-1-one (8g): pate yellow solid; yield 75%; mp 141.4-142.6 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.64-3.83 (8H, m, piperazine), 6.65-6.68 (2H, m, pyridine 3, 5-H), 6.91 (1H, d, *J* = 15.4 Hz, PhCH=C*H*), 7.34-7.41 (3H, m, Ph 2, 6-H, pyridine 4-H), 7.49-7.55 (3H, m, Ph 3, 4, 5-H), 7.71 (1H, d, *J* = 15.7 Hz, PhC*H*=CH), 8.21 (1H, dd, *J* = 5.5 and 1.8 Hz, pyridine 6-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 41.7, 41.8, 45.2, 107.1, 113.8, 117.0, 127.7, 128.8, 129.7, 135.2, 137.6, 143.0, 148.0, 159.0, 165.6; MS (EI) *m/z*: 293 (M^+, 78), 162 (23), 133 (89), 131 (35), 120 (47), 107 (100), 103 (31).; HRMS (EI) *m/z*: 293.1528 (Calcd for $C_{18}H_{19}N_3O$, 293.1528).

6-Methoxy-4-(4-phenylpiperazin-1-yl)benzo[*b*]furo[3,2-*b*]pyridine (2h): PTLC with [$CHCl_3$/AcOEt (5:2)]; pale yellow solid; yield 49%; mp 232.0-233.4 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.41-3.43 (4H, m, piperazine-H), 3.84-3.87 (4H, m, piperazine-H), 4.05 (3H, s, OCH_3), 6.73 (1H, d, *J* = 5.9 Hz, 3-H), 6.89-6.94 (1H, m, Ph-H), 6.99-7.05 (3H, m, 7-H, Ph-H), 7.28-7.34 (3H, m, 8-H, Ph-H), 7.78 (1H, d, *J* = 7.3 Hz, 9-H), 8.38 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 48.0, 49.2, 56.2, 107.0, 110.7, 113.0, 116.5, 117.1, 120.3, 124.0, 125.4, 129.2, 142.3, 144.5, 145.4, 145.7, 146.7, 151.1; IR (KBr) ν: 1638, 1587, 1492, 1236, 990 cm^{-1}; MS (EI) *m/z*: 359 (M^+, 100), 226 (33), 132 (70), 105 (50), 77 (13); Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.32; H, 5.87; N, 11.48.

4-(4-(4-Fluorophenyl)piperazin-1-yl)-6-methoxybenzo[*b*]furo[3,2-*b*]pyridine (2i): PTLC with [$CHCl_3$/AcOEt (5:2)]; whote solid; yield 66%; mp 202.6-203.8 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.35 (4H, t, *J* = 5.1 Hz, piperazine), 3.87 (4H, t, *J* = 5.1 Hz, piperazine), 4.06 (3H, s, OCH_3), 6.74 (1H, d, *J* = 5.9 Hz, 3-H), 6.93-7.03 (4H, m, Ph-H), 7.06 (1H, dd, *J* = 8.1 and 0.8 Hz, 7-H), 7.33 (1H, t, *J* = 7.9 Hz, 8-H), 7.78 (1H, dd, *J* = 7.7 and 1.1 Hz, 9-H), 8.39 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 48.1, 50.3, 56.2, 107.0, 110.7, 113.1, 115.7, 118.4, 124.1, 125.3, 140.0, 142.3, 144.5, 145.4, 145.7, 146.6, 147.8, 157.6; IR (KBr) ν: 1591, 1516, 1273, 1236, 1202 cm^{-1}; MS (EI) *m/z*: 377 (M^+, 100), 253 (8), 226 (28), 150 (48), 123 (36); Anal. Calcd for $C_{22}H_{10}FN_3O_2 \cdot 1/4\ H_2O$: C, 69.19; H, 5.41; N, 11.00. Found: C, 69.46; H, 5.55; N, 10.98.

(*E*)-1-(4-(4-Fluorophenyl)piperazin-1-yl)-3-phenylprop-2-en-1-one (8i): pale yellow solid; yield 77%;

mp 170.0-172.5 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.13-3.15 (4H, m, piperazine), 3.85 (4H, br s, piperazine), 6.87-6.92 (3H, m, PhCH=C*H*, Ph-H), 6.96-7.01 (2H, m, Ph-H), 7.34-7.41 (3H, m, Ph-H), 7.52-7.55 (2H, m, Ph-H), 7.70 (1H, d, *J* = 15.4 Hz, PhC*H*=CH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 42.2, 45.9, 50.5, 50.8, 115.6, 115.8, 116.9, 118.5, 118.6, 127.7, 128.8, 129.7, 135.2, 143.1, 147.6, 147.6, 156.4, 158.8, 165.5; MS (EI) *m/z*: 310 (M^+, 86), 179 (27), 150 (100), 131 (21), 103 (19); HRMS (EI) *m/z*: 310.1480 (Calcd for $C_{19}H_{19}FN_2O$, 310.1481).

4-(4-(2-Fluorophenyl)piperazin-1-yl)-6-methoxybenzo[*b*]furo[3,2-*b*]pyridine (2j): PTLC with [$CHCl_3$/AcOEt (5:2) and hexane/AcOEt (1:50)]; pale yellow solid; yield 57%; mp 165.5-168.5 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.33 (4H, t, *J* = 5.0 Hz, piperazine), 3.87 (4H, t, *J* = 5.0 Hz, piperazine), 4.05 (3H, s, OCH_3), 6.74 (1H, d, *J* = 5.5 Hz, 3-H), 6.95-7.11 (4H, m, Ph-H), 7.04 (1H, dd, *J* = 8.0 and 0.9 Hz, 7-H), 7.32 (1H, t, *J* = 7.9 Hz, 8-H), 7.78 (1H, dd, *J* = 7.7 and 1.1 Hz, 9-H), 8.38 (1H, d, *J* = 5.9 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 48.2, 50.4, 50.4, 56.2, 107.0, 110.7, 113.0, 116.1, 116.4, 119.1, 119.1, 122.9, 123.9, 124.0, 124.5, 124.6, 125.4, 139.7, 139.9, 140.0, 142.4, 144.5, 145.4, 145.7, 146.7, 154.6, 157.1; IR (KBr) ν: 2833, 1597, 1499, 1270, 1198, 990 cm^{-1}; MS (EI) *m/z*: 377 (M^+, 100), 226 (36), 150 (58); Anal. Calcd for $C_{22}H_{20}FN_3O_2 \cdot 3/10\ H_2O$: C, 68.94; H, 5.42; N, 11.01. Found: C, 67.22; H, 5.34; N, 10.82.

(*E*)-1-(4-(2-Fluorophenyl)piperazin-1-yl)-3-phenylprop-2-en-1-one (8j): pale yellow solid; yield 89%; mp 111.6-112.6 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.11 (4H, t, *J* = 5.1 Hz, piperazine), 3.84-3.89 (4H, m, piperazine), 6.91 (1H, d, *J* = 15.4 Hz, PhCH=C*H*), 6.91-7.09 (4H, m, Ph-H), 7.32-7.40 (3H, m, Ph 3, 4, 5-H), 7.50-7.56 (2H, m, Ph 2, 6-H), 7.70 (1H, d, *J* = 15.4 Hz, PhC*H*=CH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 42.3, 46.1, 50.4, 51.1, 116.2, 116.4, 117.0, 119.3, 119.3, 123.1, 123.2, 124.5, 124.6, 127.7, 128.8, 129.7, 135.3, 139.5, 139.6, 143.0, 154.6, 157.1, 165.5; MS (EI) *m/z*: 310 (M^+, 63), 150 (100), 131 (17), 103 (18); HRMS (EI) *m/z*: 310.1481 (Calcd for $C_{19}H_{19}FN_2O$, 310.1481).

6-Methoxy-4-(*N*,*N*-diethylamino)benzo[*b*]furo[3,2-*b*]pyridine (2k): PTLC with [$CHCl_3$/AcOEt (5:2)]; yellow oil; yield 64%; ^{1}H-NMR (400 MHz ; $CDCl_3$) δ: 1.32 (6H, t, *J* = 7.3 Hz, CH_2CH_3), 3.73(4H, q, *J* = 7.3 Hz, CH_2CH_3), 4.05 (3H, s, OCH_3), 6.51 (1H, d, *J* = 5.8 Hz, 3-H), 7.01 (1H, dd, *J* = 8.0 and 1.1 Hz, 7-H), 7.29 (1H, t, *J* = 8.1 Hz, 8-H), 7.77 (1H, dd, *J* = 8.8 and 1.1 Hz, 9-H), 8.25 (1H, d, *J* = 5.9 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 13.3, 45.4, 56.4, 105.1, 110.8, 113.1, 123.6, 125.6, 138.4, 140.8, 143.8, 145.2, 145.6, 146.2; IR (KBr) ν: 2969, 1597, 1434, 1202, 1069 cm^{-1}; MS (EI) *m/z*: 270 (M^+, 25), 255 (58), 156 (49), 91 (50), 61 (100), 43 (56); Anal. Calcd for $C_{16}H_{18}N_2O_2 \cdot 1/2\ H_2O$: C, 68.80; H, 6.96; N, 10.03. Found: C, 68.80; H, 6.78; N, 9.86.

6-Methoxy-4-(*N*-pyridin-4-ylmethylamino)benzo[*b*]furo[3,2-*b*]pyridine (2l): PTLC with [$CHCl_3$/MeOH (10:1) and (10:3)]; brown oil; yield 45%; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.07 (3H, s,

OCH_3), 4.61 (2H, d, *J* = 5.8 Hz, CH_2), 5.38 (1H, t, *J* = 5.9 Hz, NH), 6.46 (1H, d, *J* = 5.5 Hz, 3-H), 7.06 (1H, dd, *J* = 8.1 and 0.8 Hz, 7-H), 7.31 (2H, d, *J* = 5.9 Hz, 3',5'-H), 7.34 (1H, t, *J* = 7.9 Hz, 8-H), 7.78 (1H, dd, *J* = 7.9 and 0.9 Hz, 9-H), 8.29 (1H, d, *J* = 5.5 Hz, 2-H), 8.60 (2H, dd, *J* = 4.4 and 0.8 Hz, 2',6'-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 45.88, 56.18, 103.25, 110.26, 113.25, 121.90, 124.20, 125.78, 138.49, 139.34, 142.83, 145.65, 145.68, 146.89, 146.93, 150.26; IR (KBr) ν: 3256, 1642, 1611, 1345, 1198, 1055 cm^{-1}; MS (EI) *m/z*: 305 (M^+, 100), 227 (37), 212 (18), 186 (17); Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.68; H, 4.99; N, 13.54.

6-Methoxy-4-(*N*-thiophen-2-ylmethylamino)benzo[*b*]furo[3,2-*b*]pyridine (2m): PTLC with [$CHCl_3$/AcOEt (1:1)]; yellow solid; yield 65%; mp 160.4-163.3 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.05 (3H, s, OCH_3), 4.73 (2H, dd, *J* = 5.4 and 0.7 Hz, CH_2), 5.24 (1H, t, *J* = 5.4 Hz, NH), 6.66 (1H, d, *J* = 5.4 Hz, 3-H), 6.98 (1H, dd, *J* = 5.1 and 3.3 Hz, thiophene-H), 7.03 (1H, dd, *J* = 8.0 and 0.7 Hz, 7-H), 7.06-7.07 (1H, m, thiophene-H), 7.25 (1H, dd, *J* = 5.1 and 1.5 Hz, thiophene-H), 7.32 (1H, t, *J* = 7.9 Hz, 8-H), 7.77 (1H, dd, *J* = 7.9 and 1.0 Hz, 9-H), 8.34 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 42.1, 56.2, 103.3, 110.2, 113.2, 124.1, 125.3, 125.9, 126.0, 127.1, 138.6, 139.6, 140.5, 142.7, 145.6, 145.7, 146.94; IR (KBr) ν: 3263, 1638, 1488, 1267, 1198 cm^{-1}; MS (EI) *m/z*: 310 (M^+, 71), 97 (100); Anal. Calcd for $C_{17}H_{14}N_2O_2 \cdot 1/2\ H_2O$: C, 63.93; H, 4.73; N, 8.77. Found: C, 63.89; H, 4.51; N, 8.62.

***N*-(Thiophen-2-ylmethyl)cinnamamide (8m)**: yellow solid; yield 68%; mp 115.1-118.0 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.74 (2H, d, *J* = 5.5 Hz, CH_2), 6.01 (1H, br s, NH), 6.39 (1H, d, *J* = 15.4 Hz, PhCH=C*H*), 6.95 (1H, dd, *J* = 5.2 and 3.3 Hz, thiophene-H), 7.00-7.02 (1H, m, thiophene-H), 7.23 (1H, dd, *J* = 5.2 and 1.1 Hz, thiophene-H), 7.33-7.38 (3H, m, Ph 3, 4, 5-H), 7.47-7.49 (2H, m, Ph 2, 6-H), 7.66 (1H, d, *J* = 15.4Hz, PhC*H*=CH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 38.5, 120.2, 125.3, 126.2, 126.9, 127.8, 128.8, 129.8, 134.8, 140.8, 141.6, 165.5; MS (EI) *m/z*: 243 (M^+, 100), 131 (67), 112 (20), 103 (45), 77 (29); HRMS (EI) *m/z*: 243.0720 (Calcd for $C_{14}H_{13}NOS$, 243.0718).

6-Methoxy-4-(*N*-phenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2n): PTLC with [$CHCl_3$/AcOEt (10:1)]; cream solid; yield 94%; mp 147.6-149.7 °C; ^{1}H-NMR (400 MHz; $CDCl_3$) δ: 4.09 (3H, s, OCH_3), 6.71 (1H, s, NH), 7.08 (1H, dd, *J* = 8.7 and 0.7 Hz, 7-H), 7.13 (1H, d, *J* = 5.9 Hz, 3-H), 7.18 (1H, t, *J* = 8.4 Hz, 8-H), 7.31-7.44 (5H, m, Ph-H), 7.80 (1H, dd, *J* = 7.7 and 0.7 Hz, 9-H), 8.35 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.2, 104.5, 110.4, 113.2, 121.5, 124.2, 124.3, 125.8, 129.6, 136.6, 138.9, 139.1, 143.5, 145.6, 145.7, 146.7; IR (KBr) ν: 3406, 1638, 1601, 1502, 1430, 1273 cm^{-1}; MS (EI) *m/z*: 290 (M^+, 100), 289 (11), 219 (7), 247 (5); Anal. Calcd for $C_{18}H_{14}N_2O_2 \cdot 1/3\ H_2O$: C, 72.96; H, 4.99; N, 9.45. Found: C, 72.92; H, 4.74; N, 9.25.

6-Methoxy-4-(*N*-4-fluorophenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2o): PTLC with [$CHCl_3$/AcOEt (5:2)]; reddish brown solid; yield 50%; mp 160.2-163.9 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.09 (3H, s,

OCH_3), 6.60 (1H, br s, NH), 6.95 (1H, d, *J* = 5.5 Hz, 3-H), 7.07-7.14 (3H, m, 7, 3', 5'-H), 7.29 (2H, dd, *J* = 9.0 and 4.6 Hz, 2', 6'-H), 7.36 (1H, t, *J* = 7.9 Hz, 8-H), 7.80 (1H, dd, *J* = 7.3 and 0.7 Hz, 9-H), 8.34 (1H, d, *J* = 5.9 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.2, 104.2, 110.5, 113.3, 116.5, 124.3, 124.3, 125.8, 134.9, 137.1, 138.8, 143.6, 145.7, 145.8, 146.8, 159.9; IR (KBr) ν: 3645, 1642, 1560, 1509, 1273, 1205 cm^{-1}; MS (EI) *m/z*: 308 (M^+, 100.00), 293 (6.36), 237 (10.89); Anal. Calcd for $C_{18}H_{13}FN_2O_2$: C, 70.12; H, 4.25; N, 9.09. Found: N, 69.99; H, 4.11; N, 9.01.

6-Methoxy-4-(*N*-4-chlorophenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2p): PTLC with [$CHCl_3$/AcOEt(1:1)]; pale orange solid; yield 50%; mp 186.5-187.9 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.09 (3H, s, OCH_3), 6.66 (1H, br s, NH), 7.07 (1H, d, *J* = 5.9 Hz, 3-H), 7.09 (1H, dd, *J* = 8.0 and 1.1 Hz, 7-H), 7.26 (2H, d, *J* = 8.8 Hz, 2', 6'-H), 7.35-7.39 (3H, m, 8, 3', 5'-H), 7.80 (1H, dd, *J* = 7.9 and 1.0 Hz, 9-H), 8.37 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.3, 104.7, 110.6, 113.3, 122.7, 124.3, 125.8, 129.5, 129.7, 136.2, 137.8, 139.0, 143.9, 145.7, 145.8, 146.8; IR (KBr) ν: 3329, 1642, 1594, 1492, 1386, 1198 cm^{-1}; MS (EI) *m/z*: 326 (M+2, 33), 324 (M^+, 100), 309 (5), 289 (2); Anal. Calcd for $C_{18}H_{13}BrN_2O_2$: C, 58.56; H, 3.55; N, 7.59. Found: C, 58.42; H, 3.55; N, 7.46.

6-Methoxy-4-(*N*-4-bromophenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2q): PTLC with [$CHCl_3$/AcOEt (10:1)]; yellow solid; yield 51%; mp 40.0-42.0 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.09 (3H, s, OCH_3), 6.66 (1H, br s, NH), 7.08-7.10 (2H, m, 3, 7-H), 7.20 (2H, d, *J* = 8.8 Hz, 2', 6'-H), 7.37 (1H, t, *J* = 8.1 Hz, 8-H), 7.52 (2H, d, *J* = 8.8 Hz, 3', 5'-H), 7.80 (1H, dd, *J* = 7.8 and 0.9 Hz, 9-H), 8.37 (1H, d, *J* = 5.1 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.2, 104.7, 110.5, 113.3, 116.9, 122.9, 124.3, 125.7, 132.7, 136.0, 138.3, 139.0, 143.9, 145.7, 145.8, 146.8; IR (KBr) ν: 3270, 1649, 1580, 1488, 1273, 1195 cm^{-1}; MS (EI) *m/z*: 370 (M+2, 98), 368 (M^+, 100), 289 (9); Anal. Calcd for $C_{18}H_{13}FN_2O_2 \cdot 3/4\ H_2O$: C, 67.18; H, 4.54; N, 8.70. Found: C, 69.86; H, 4.52; N, 8.56.

6-Methoxy-4-(*N*-3-fluorophenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2r): PTLC with [$CHCl_3$/AcOEt (10:1)]; pale yellow solid; yield 65%; mp 141.6-145.8 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.08 (1H, s, OCH_3), 6.79 (1H, br s, NH), 6.82-6.87 (1H, m, 4'-H), 7.03 (3H, m, 7-H and 5', 6'-H), 7.18 (1H, d, *J* = 5.5 Hz, 3-H), 7.32-7.38 (2H, m, 8, 2'-H), 7.79 (1H, dd, *J* = 7.9 and 1.0 Hz, 9-H), 8.40 (1H, d, *J* = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 56.2, 105.1, 107.9, 110.6, 110.8, 113.3, 116.4, 124.4, 125.7, 130.8, 135.7, 139.0, 141.0, 143.9, 145.7, 145.8, 146.7, 163.5; IR (KBr) ν: 3031, 1645, 1594, 1492, 1434, 1202 cm^{-1}; MS (EI) *m/z*: 308 (M^+, 100), 237 (12); Anal. Calcd for $C_{18}H_{13}FN_2O_2 \cdot 3/4\ H_2O$; C, 67.18; H, 4.54; N, 8.70. Found: C, 69.86; H, 4.52; N, 8.56.

6-Methoxy-4-(*N*-methyl-*N*-phenylamino)benzo[*b*]furo[3,2-*b*]pyridine (2s): PTLC with [$CHCl_3$/AcOEt (10:1)]; pale yellow solid; yield 63%; mp 64.9-67.3 ˚C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.75 (3H, s, NCH_3), 3.91 (3H, s, OCH_3), 6.68 (1H, d, *J* = 5.5 Hz, 3-H), 7.02 (1H, dd, *J* = 7.9 and 1.0 Hz, 7-H),

7.20-7.26 (3H, m, 2', 4', 6'-H), 7.30 (1H, t, J = 7.9 Hz, 8-H), 7.40 (1H, dd, J = 8.4 and 7.3 Hz, 3', 5'-H), 7.77 (1H, dd, J = 7.9 and 0.9 Hz, 9-H), 8.28 (1H, d, J = 5.5 Hz, 2-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 40.9, 56.7, 109.5, 112.1, 113.1, 123.9, 124.3, 125.1, 125.6, 129.5, 139.8, 141.0, 144.8, 145.5, 145.6, 146.1, 146.9; IR (KBr) ν: 3399, 1594, 1495, 1389, 1273 cm^{-1}; MS (EI) *m/z*: 304 (M^+, 100), 288 (4); Anal. Calcd for $C_{19}H_{16}N_2O_2 \cdot 3/5H_2O$: C, 72.41; H, 5.50; N, 8.89. Found: C, 72.51; H, 5.34; N, 8.86.

ACKNOWLEDGEMENTS

The authors thank the staff of the Instrument Analysis Center of Mukogawa Women's University for the ^{1}H-NMR and MS measurements and elemental analyses.

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